

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-360

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-360

NAME OF APPLICANT / NDA HOLDER

GlaxoSmithKline, LP

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

Nicorette

ACTIVE INGREDIENT(S)

Nicotine Polacrilex

STRENGTH(S)

2mg

DOSAGE FORM

Lozenge, Oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(o)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: if additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

5,110,605

b. Issue Date of Patent

5/5/1992

c. Expiration Date of Patent

8/21/2010

d. Name of Patent Owner

Watson Pharmaceuticals, Inc.

Address (of Patent Owner)

311 Bonnie Circle

City/State

Corona, California

ZIP Code

92880

FAX Number (if available)

Telephone Number

951-493-5300

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (i)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

Nora Stein

5/15/09.

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Nora L. Stein, Esq

Address

709 Swedeland Road, UW2220

City/State

King of Prussia, Pennsylvania

ZIP Code

19406

Telephone Number

610-270-5044

FAX Number (if available)

610-270-5090

E-Mail Address (if available)

Nora.Stein@gsk.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-360

NAME OF APPLICANT / NDA HOLDER

GlaxoSmithKline, LP

The following is provided in accordance with Section 305(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

Nicorette

ACTIVE INGREDIENT(S)

Nicotine Polacrifex

STRENGTH(S)

4mg

DOSAGE FORM

Lozange, Oral

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1. GENERAL

a. United States Patent Number 5,110,605	b. Issue Date of Patent 5/5/1992	c. Expiration Date of Patent 8/21/2010
d. Name of Patent Owner Watson Pharmaceuticals, Inc.	Address (of Patent Owner) 311 Bonnie Circle	
	City/State Corona, California	
	ZIP Code 92880	FAX Number (if available)
	Telephone Number 951-493-5300	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 305(b)(3) and (i)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.55 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.a.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		

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2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

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2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

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Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

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Date Signed

Nora Stein

5/15/09

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Nora L. Stein, Esq

Address

709 Swedeland Road, UW2220

City/State

King of Prussia, Pennsylvania

ZIP Code

19406

Telephone Number

610-270-5044

FAX Number (if available)

610-270-5090

E-Mail Address (if available)

Nora.Stein@gsk.com

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Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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EXCLUSIVITY SUMMARY

NDA # 22-360

SUPPL #

HFD # 560

Trade Name Nicorette mini lozenge

Generic Name nicotine polacrilex

Applicant Name GlaxoSmithKline

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

According to the Clinical Pharmacology review all studies were designed to assess the bioequivalence between the Nicorette mini (nicotine polacrilex) lozenge and the original Commit (nicotine polacrilex) lozenge (NDA 21-330) and studies were found to be bioequivalent.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21-330

Commit lozenge, 2mg and 4 mg nicotine polirilex

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

YES
Explain:

! NO
! Explain:

Investigation #2

!

!

YES
Explain:

! NO
! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

Name of person completing form: Mary M. Lewis
Title: Regulatory Project Manager
Date: May 18, 2009

Name of Office/Division Director signing form:
Title:

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Mary Lewis
5/18/2009 02:07:49 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-360 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: 7/18/08 PDUFA Goal Date: 5/18/09

HFD 560 Trade and generic names/dosage form: Commit Mini Mint (nicotine polacrilex) Lozenge, 2 mg and 4 mg

Applicant: GlaxoSmithKline Therapeutic Class: 2030700

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- X Yes. Please proceed to the next question.
- No. PREA does not apply. Skip to signature block.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: **Reduction of withdrawal symptoms, including nicotine craving associated with quitting smoking.**

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- X No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- X No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 10 Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: Sponsor views 0-10 years to be inappropriate for treatment with nicotine replacement therapy (NRT) particularly in the OTC setting. Also, this age range represents a small population with significant nicotine dependence.

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 10 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 17 Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: Please see attached Request for Deferral of Pediatric Studies from the sponsor on page 4 of this Peds Page form.

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

NDA 22-360

Page 3

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

(Attachment: on next page, page 4)

Request for Deferral of Pediatric Studies

NDA Number: NDA 22-360

Sponsor: GlaxoSmithKline Consumer Healthcare

Indication: reduce withdrawal symptoms, including nicotine craving associated with quitting smoking

(a) Is the indication for life-threatening condition that occurs in the pediatric population? No

(b) If yes, are there approved therapies labeled for use in the pediatric population? Not applicable

(c) If yes, list the approved therapies and labeled pediatric age groups of approval Not applicable

1. What are the ages included in your deferral request?

Ages ≥ 10 to 17 years

Reasons for not including the entire pediatric population in the studies or in the deferral request?

Waiver request for pediatric population below Age 10.

2. Reasons for deferring pediatric studies:

Among the conditions of approval of NDA 21-330 was that GSK conduct a pediatric study for patients 10-17 years. GSK conducted and submitted the study to FDA on August 21, 2007

That study is currently under review by the Agency.

Based on the bioequivalence of the proposed Nicotine Mini Mint Lozenges to the originally approved Commit Lozenges, GSK believes that the study could cover similar issues in the new formulation. Therefore, we request a deferral pending the completion of the Agency's review of the study.

b(4)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Mary Lewis

10/1/2008 11:58:13 AM

Debarment Certification

Pursuant to Section 306(a) and (b) of the Federal Food, Drug, and Cosmetic Act [21 USC 335(a) and (b)], and to the best of my information, knowledge and belief, no one involved in the development of this New Drug Application who has been or is currently employed by GlaxoSmithKline Consumer Healthcare, has been debarred. Additionally, there are no debarment procedures pending for any current or past employees of GlaxoSmithKline Consumer Healthcare. This was determined by comparing the current debarment list, dated November 7, 2007, to the listing of past and present GlaxoSmithKline Consumer Healthcare employees.

Further, we certify GlaxoSmithKline Consumer Healthcare will not use the services in any capacity of anyone debarred by the United States Food and Drug Administration.

We are not aware of any relevant convictions of GlaxoSmithKline Consumer Healthcare personnel for which an individual can be debarred as described in section 306(a) and (b).



Bruce V. Hicks
Assistant General Counsel


Date

Financial Information

**21 CFR § 54.4(a)(1) and (3)
21 CFR 314.50(k)**

Financial Disclosure

In accordance with 21 CFR 54.4(a)(3) all clinical investigators that were involved in the conduct of a study as part of this new drug application were evaluated to determine whether completion of Form FDA 3455, disclosing any financial interests and arrangements as defined in 21 CFR 54.2, was required. GlaxoSmithKline has determined that this section is not applicable as no investigator has satisfied the requirements of this section.

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	See Attached	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Iris H. Shelton	TITLE Assistant Director, Regulatory Affairs
FIRM/ORGANIZATION GlaxoSmithKline Consumer Healthcare	
SIGNATURE 	DATE 7/18/08

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room MC-03
Rockville, MD 20857

1 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

MEMORANDUM OF TELECON

DATE: April 14, 2009

APPLICATION NUMBER: NDA 22-360

BETWEEN:

GlaxoSmithKline

Iris H. Shelton, Assistant Director, Regulatory Affairs

David Schiffkovitz, Director, Regulatory Affairs

Erin Oliver, Director, Regulatory Affairs

Phone: 800-988-9755

AND

Office of Nonprescription Products

Leah Christl, Ph.D., Associate Director, Regulatory Affairs

Division of Nonprescription Clinical Evaluation:

Andrea Leonard-Segal, MD, Director

Joel Schiffenbauer, M.D., Deputy Director

Melissa Hancock Furness, Chief, Project Management Staff

Priscilla Callahan-Lyon, M.D., medical reviewer

Mary Lewis, R.N., Regulatory Project Manager

Larry Bauer, R.N., M.S., Regulatory Project Manager

Cindy Li, Ph.D., Pharmacology/Toxicology Reviewer

Division of Nonprescription Regulation Development:

Mary Robinson, M.S., Interdisciplinary Scientist Reviewer

Debbie Lumpkins, Interdisciplinary Scientist Team Leader

Division of Medication Error Prevention & Analysis:

Zachary Oleszczuk, PharmD, Safety Evaluator

SUBJECT: Labeling discussion

On April 14, 2009 an email transmittal was sent to GlaxoSmithKline (GSK) listing the following comments in response to GSK's February 10, 2009 submission of labeling for Nicorette Lozenge (mini), NDA 22-360. In that email we recommended that GSK make the following changes to:

Principal Display Panel:

1. The statement of identity is presented in a small size as compared to the proprietary name. We request you revise the size of the established name so that it appears in a size reasonably related to the most prominent printed matter on the principal display panel.

GSK agreed with the above.

Container Label (2 mg and 4 mg)

2. The strength on the container label is hard to see because it is embedded in the established name in a small font. Once the container is removed from the carton it is difficult to identify the strength of the product. We request you increase the size and prominence of the strength on the container label so the strength can be easily identified.

GSK agreed with the above.

Carton Side Panel

3. Under “To increase your success in quitting”:
 - a. Paragraph 2. Insert the word “lozenge” after the word “mini” to complete the form descriptor.

GSK proposed to modify the statement to read: “Use enough- Use at least 9 Nicorette mini lozenges per day during the first six weeks”

The Agency agreed this was acceptable.

- b. Paragraph 3. Insert the word “lozenge” after the word “mini” to complete the form descriptor.

GSK agreed with the above.

Vial 24 and 27 count

4. Decrease the font size of the word “mini” in the form descriptor “mini lozenge”. Make “mini” and “lozenge” the same size on the front of the 24 and 27 count vials.

GSK stated their belief that the presentation of the form descriptor “mini lozenge” is part of trade dress and not subject to any regulatory requirement. FDA noted that as currently presented, the form descriptor distracted from the required prominence of the statement of

identity. FDA stated there was insufficient balance in the size relationship between the brand name, statement of identity and the form descriptor. GSK agreed to take this into consideration and revise the labels by increasing the prominence of the statement of identity where ever it appears in labeling. It was agreed that the font size for "mini" and "lozenge" did not have to be identical as long as the above mentioned revisions to increase the prominence of the statement of identity were incorporated into the label.

User Guide

5. Cover page. Capitalize the letter "M" in the word "mini" in the following heading:

"How to Use Nicorette Mini Lozenges and Tips to Help you Quit Smoking".

GSK agreed with the above.

6. The word "mini" is part of the form descriptor name. Unbold the word "mini" and capitalize the "M" wherever the words "Mini Lozenges" appear in the User's Guide. Also, make the words "mini" and "lozenge" the same font and size throughout the Guide.

GSK wants to keep it the way it is and FDA agreed. See discussion in 4 above.

7. Page 3, paragraph 2, line 7: Delete the 2nd word '——' in the paragraph. —— is not part of the Trade Name. Alternatively, the word "Lozenge" could be added and the word "mini" unbolded and capitalized. b(4)

GSK said that they would revise the sentence to remove the second —— . FDA found the proposed revision acceptable. b(4)

8. Page 5, paragraph 3, bullet 1. Delete the phrase ————— . The phrase is not required according to § 201.64(c) and it is not included in the proposed "Drug Facts" carton labeling. b(4)

GSK agreed with the above.

The t-con was held from 1:30 p.m. to 2:00 p.m.

Mary M. Lewis, RPM

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Mary Lewis
5/15/2009 03:54:20 PM
CSO

Mary Lewis
5/15/2009 03:55:05 PM
CSO

Lewis, Mary

From: Furness, Melissa
Sent: Friday, May 15, 2009 1:38 PM
To: Schiffenbauer, Joel; Lewis, Mary
Subject: FW: N22-360

Melissa

From: Tang, Yubing
Sent: Friday, May 15, 2009 1:26 PM
To: Tang, Yubing; Furness, Melissa
Cc: Stock, Marisa; Johnson, Elizabeth; Ding, Shulin; Goldie, Scott
Subject: RE: N22-360

Sorry. I meant "addendum".

Yubing

Yubing Tang, Ph. D.

CMC Reviewer

U.S. Food and Drug Administration

White Oak #22/Rm. 1481

10909 New Hampshire Ave.

Silver Spring, MD 20993

Tel: 301-796-2457

Fax: 301-796-9860

yubing.tang@fda.hhs.gov

From: Tang, Yubing
Sent: Friday, May 15, 2009 1:24 PM
To: Furness, Melissa
Cc: Stock, Marisa; Johnson, Elizabeth; Ding, Shulin; Goldie, Scott
Subject: RE: N22-360

Melissa,

FYI. And I will get CMC amendment ready soon.

Yubing

Yubing Tang, Ph. D.

CMC Reviewer

U.S. Food and Drug Administration

White Oak #22/Rm. 1481

5/18/2009

10903 New Hampshire Ave.

Silver Spring, MD 20993

Tel: 301-796-9457

Fax: 301-796-9850

yubing.tang@fda.hhs.gov

From: Johnson, Elizabeth
Sent: Friday, May 15, 2009 1:21 PM
To: Tang, Yubing; Ding, Shulin; Goldie, Scott
Cc: Stock, Marisa
Subject: N22-360

Good afternoon,

NDA 22-360 has just been given and overall acceptable compliance recommendation.

Thanks,

Beth

Elizabeth L. Johnson
Consumer Safety Officer
FDA/CDER/OC/DMPQ
10903 New Hampshire Avenue
White Oak, Bldg. 51, Rm. 4225
Silver Spring, MD 20993
Phone: (301) 796-3334
Fax: (301) 847-8738

5/18/2009

NDA/BLA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

Application Information	
NDA # 22-360 BLA#	NDA Supplement #:S- BLA STN #
Efficacy Supplement Type SE-	
Proprietary Name: Nicorette Mini Lozenge Established/Proper Name: nicotine polacrilex Dosage Form: lozenge Strengths: 2 mg and 4 mg	
Applicant: GlaxoSmithKline Agent for Applicant (if applicable):	
Date of Application: 7/18/08 Date of Receipt: 7/18/08 Date clock started after UN:	
PDUFA Goal Date: 5/18/09	Action Goal Date (if different):
Filing Date: 9/29/08 Date of Filing Meeting: 9/9/08	
Chemical Classification: (1,2,3 etc.) (original NDAs only) 5	
Proposed Indication(s): Reduction of withdrawal symptoms, including nicotine craving associated with quitting smoking.	
Type of Original NDA: AND (if applicable) Type of NDA Supplement:	<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>Refer to Appendix A for further information.</i>	
Review Classification: <i>If the application includes a complete response to pediatric WR, review classification is Priority.</i> <i>If a tropical disease Priority review voucher was submitted, review classification defaults to Priority.</i>	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority <input type="checkbox"/> Tropical disease Priority review voucher submitted
Resubmission after withdrawal? <input type="checkbox"/>	
Resubmission after refuse to file? <input type="checkbox"/>	
Part 3 Combination Product? <input type="checkbox"/>	<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device <input type="checkbox"/> PMC response <input type="checkbox"/> PMR response:
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC Other:	<input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR

601.42)	
Collaborative Review Division (if OTC product): Division of Nonprescription Regulation Development	
List referenced IND Number(s): 56,295 and NDA 21-330	
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established name to the supporting IND(s) if not already entered into tracking system.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are all classification codes/flags (e.g. orphan, OTC drug, pediatric data) entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Application Integrity Policy	
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: http://www.fda.gov/ora/compliance_ref/ainlist.html</i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
If yes, explain:	
If yes, has OC/DMPQ been notified of the submission?	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
User Fee Status	
Form 3397 (User Fee Cover Sheet) submitted	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
User Fee Status	<input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. It is expected that all 505(b) applications, whether 505(b)(1) or 505(b)(2), will require user fees unless otherwise waived or exempted (e.g., business waiver, orphan exemption).</i>	
Comments	

<p>Does another product have orphan exclusivity for the same indication? Check the Electronic Orange Book at: http://www.fda.gov/cder/ob/default.htm</p> <p>If yes, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?</p> <p>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</p> <p>Comments:</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (NDAs/NDA efficacy supplements only)</p> <p>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</p> <p>Comments:</p>	<input type="checkbox"/> YES # years requested: <input checked="" type="checkbox"/> NO
<p>If the proposed product is a single enantiomer of a racemic drug previously approved for a different therapeutic use (NDAs only):</p> <p>Did the applicant (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b) request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?</p> <p>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</p>	<input checked="" type="checkbox"/> Not applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Section 505(b)(2) (NDA/NDA efficacy supplements only)	
<p>1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p> <p>2. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).</p> <p>3. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?</p>	<input checked="" type="checkbox"/> Not applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO

Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).

4. Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? *Check the Electronic Orange Book at: <http://www.fda.gov/cder/ob/default.htm>*

YES
 NO

If yes, please list below:

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.

Content of Content

Do not check mixed submission if the only electronic component is the content of labeling (COL).

Comments:

All paper (except for COL)
 All electronic
 Mixed (paper/electronic)

CTD
 Non-CTD
 Mixed (CTD/non-CTD)

If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?

If electronic submission: paper forms and certifications signed (non-CTD) or electronic forms and certifications signed (scanned or digital signature)(CTD)?

YES
 NO

Forms include: 356h, patent information (3542a), financial disclosure (3454/3455), user fee cover sheet (3542a), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.

Comments:

If electronic submission, does it follow the eCTD guidance? (<http://www.fda.gov/cder/guidance/7087rev.pdf>)

YES
 NO

If not, explain (e.g., waiver granted):

<p>Form 356h: Is a signed form 356h included?</p> <p><i>If foreign applicant, both the applicant and the U.S. agent must sign the form.</i></p> <p>Are all establishments and their registration numbers listed on the form?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Index: Does the submission contain an accurate comprehensive index?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Controlled substance/Product with abuse potential:</p> <p>Abuse Liability Assessment, including a proposal for scheduling, submitted?</p> <p>Consult sent to the Controlled Substance Staff?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>BLAs/BLA efficacy supplements only:</p> <p>Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Patent Information (NDA/NDA efficacy supplements/BLAs/BLA efficacy supplements)</p>	
<p>Patent information submitted on form FDA 3542a?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Debarment Certification</p>	
<p>Correctly worded Debarment Certification with authorized signature?</p> <p><i>If foreign applicant, both the applicant and the U.S. Agent must</i></p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>

<p><i>sign the certification.</i></p> <p><i>Note: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge..."</i></p> <p>Comments:</p>	
Field Copy Certification (NDA/IND/efficacy supplements only)	
<p>Field Copy Certification: that it is a true copy of the CMC technical section (<i>applies to paper submissions only</i>)</p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<p><input checked="" type="checkbox"/> Not Applicable (<i>electronic submission or no CMC technical section</i>)</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Financial Disclosure	
<p>Financial Disclosure forms included with authorized signature?</p> <p><i>Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Pediatric	
<p>PREA</p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p> <p>Are the required pediatric assessment studies or a full waiver of pediatric studies included?</p> <p>If no, is a request for full waiver of pediatric studies OR a request for partial waiver/deferral and a pediatric plan included?</p> <ul style="list-style-type: none"> • <i>If no, request in 74-day letter.</i> • <i>If yes, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3)</i> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>

BPCA (NDAs/NDA efficacy supplements only):	
Is this submission a complete response to a pediatric Written Request? <i>If yes, contact PMHS (pediatric exclusivity determination by the Pediatric Exclusivity Board is needed).</i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Comments:	
Prescription Labeling	
Check all types of labeling submitted. Comments:	<input checked="" type="checkbox"/> Not applicable <input type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use <input type="checkbox"/> MedGuide <input type="checkbox"/> Carton labels <input type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)
Is electronic Content of Labeling submitted in SPL format? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Package insert (PI) submitted in PLR format? <i>If no, was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request?</i> <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
MedGuide or PPI (plus PI) consulted to OSE/DRISK? (<i>send WORD version if available</i>)	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
REMS consulted to OSE/DRISK?	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Carton and immediate container labels, PI, PPI, and proprietary name (if any) sent to OSE/DMEDP?	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	

OTC Labeling	
<p>Check all types of labeling submitted.</p> <p>Comments: User Guide submitted.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> Outer carton label <input checked="" type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input checked="" type="checkbox"/> Other (specify)
<p>Is electronic content of labeling submitted?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Are annotated specifications submitted for all stock keeping units (SKUs)?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>If representative labeling is submitted, are all represented SKUs defined?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>Proprietary name, all labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEDP?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Meeting Minutes and Agreements	
<p>End-of Phase 2 meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
<p>Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
<p>Any Special Protocol Assessment (SPA) agreements?</p> <p><i>If yes, distribute letter and/or relevant minutes before filing meeting.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: 9/9/08

NDA/BLA #: 22-360

PROPRIETARY/ESTABLISHED NAMES: Nicorette mini lozenge

APPLICANT: GlaxoSmithKline

BACKGROUND: GlaxoSmithKline is submitting this New Drug Application to provide a smaller version of the currently available nicotine polacrilex lozenge, Commit. The new lozenges, Nicorette 2 mg and 4 mg, are a line extension of the currently marketed Commit Lozenges, available in the same strengths and contain the same active ingredient, nicotine polacrilex. The indication is identical to the approved Commit Lozenges: reduces withdrawal symptoms, including nicotine craving associated with quitting smoking.

REVIEW TEAM:

Discipline/Organization	Name		Prescription Drug (Y/N)
Regulatory Project Management	RPM:	Mary M. Lewis	Y
	CPMS/TL:	Leah Christl, Ph.D.	Y
Cross-Discipline Team Leader (CDTL)			
Clinical	Reviewer:	Priscilla Callahan-Lyon, M.D.	Y
	TL:	Daiva Shetty, M.D.	Y
Social Scientist Review (for OTC products)	Reviewer:		
	TL:		
Labeling Review (for OTC products)	Reviewer:	Mary Robinson	Y
	TL:	Debbie Lumpkins	Y
OSE	Reviewer:		
	TL:		
Clinical Microbiology (for antimicrobial products)	Reviewer:		

	TL:		
Clinical Pharmacology	Reviewer:	Ping Ji	Y
	TL:	Srikanth Nallani	Y
Biostatistics	Reviewer:		
	TL:		
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Cindy Li	Y
	TL:	Wafa Harrouk	Y
Statistics, carcinogenicity	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Yubing Tang	Y
	TL:	Shulin Ding	Y
Facility (for BLAs/BLA supplements)	Reviewer:		
	TL:		
Microbiology, sterility (for NDAs/NDA efficacy supplements)	Reviewer:		
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:		
	TL:		
Other reviewers	Celia Winchell with DAARP		Y

OTHER ATTENDEES: Laura Shay, Social Scientist Reviewer

505(b)(2) filing issues? If yes, list issues:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Per reviewers, are all parts in English or English translation? If no, explain:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

Electronic Submission comments List comments: No comments,	<input type="checkbox"/> Not Applicable
CLINICAL Comments:	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> • Clinical study site(s) inspections(s) needed? If no, explain: 	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Advisory Committee Meeting needed? Comments: <i>If no, for an original NME or BLA application, include the reason. For example:</i> <ul style="list-style-type: none"> ○ <i>this drug/biologic is not the first in its class</i> ○ <i>the clinical study design was acceptable</i> ○ <i>the application did not raise significant safety or efficacy issues</i> ○ <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> • If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? Comments: 	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
CLINICAL MICROBIOLOGY Comments:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
CLINICAL PHARMACOLOGY	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE

Comments:	<input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
BIOSTATISTICS	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
Comments:	
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
Comments:	
PRODUCT QUALITY (CMC)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
Comments:	
<ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
<ul style="list-style-type: none"> Establishment(s) ready for inspection? <ul style="list-style-type: none"> Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? 	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Comments: Establishment had EER 7/28 - 8/1/08 and was acceptable.	
<ul style="list-style-type: none"> Sterile product? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

<p>If yes, was Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only)</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>FACILITY (BLAs only)</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

REGULATORY PROJECT MANAGEMENT

Signatory Authority: Division of Nonprescription Products

GRMP Timeline Milestones: Filing meeting: 9/9/08; Day 74: 9/29/08; Review completion goal date: 3/27/09; PDUFA goal date: 5/18/09.

Comments:

REGULATORY CONCLUSIONS/DECISIONS

<input type="checkbox"/>	<p>The application is unsuitable for filing. Explain why:</p>
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><input type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional): Application did not contain:</p> <ol style="list-style-type: none"> 1. Complete Integrated Summary of Safety 2. Information regarding local safety of the mini lozenge in the mouth 3. Lozenge counts per vial that you plant to market for the 2 mg and 4 mg mini lozenge. 4. Annotated specifications for all "Drug Facts" labels 5. A description of and manufacturing information for the tamper-evident feature <p><input checked="" type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>

ACTIONS/ITEMS

<input checked="" type="checkbox"/>	<p>Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into tracking system.</p>
<input type="checkbox"/>	<p>If RTF action, notify everybody who already received a consult request, OSE PM., and Product Quality PM. Cancel EER/TBP-EER.</p>
<input type="checkbox"/>	<p>If filed and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.</p>

<input type="checkbox"/>	
<input type="checkbox"/>	If BLA or priority review NDA, send 60-day letter.
<input checked="" type="checkbox"/>	Send review issues/no review issues by day 74
<input type="checkbox"/>	Other

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

- (1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
- (2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),
- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your OND ADRA or OND IO.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Mary Lewis
4/29/2009 04:10:55 PM
CSO

Mary Lewis
4/29/2009 04:11:04 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-360

**PROPRIETARY NAME REQUEST
- ACCEPTABLE**

GlaxoSmithKline Consumer Healthcare, L.P.
Attention: Iris H. Shelton
Assistant Director, Regulatory Affairs
1500 Littleton Road
Parsippany, New Jersey 07054-3884

Dear Ms. Shelton:

Please refer to your New Drug Application (NDA) dated July 18, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nicorette (2 mg and 4 mg, nicotine polacrilex) lozenge.

We also refer to your February 10, 2009, correspondence, received on February 10, 2009, requesting review of your proposed proprietary name, Nicorette. The Division of Medication Error Prevention and Analysis (DMEPA) have completed their review of the proposed proprietary name, Nicorette and has concluded that it is acceptable.

If any of the proposed product characteristics as stated in your February 10, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Darrell Jenkins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0558. For any other information regarding this application contact Mary Lewis, Regulatory Project Manger in the Division of Nonprescription Clinical Evaluation.

Sincerely,

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Andrea Segal
4/27/2009 04:11:54 PM

Lewis, Mary

From: Lewis, Mary
Sent: Tuesday, April 21, 2009 2:42 PM
To: 'Iris.H.Shelton@gsk.com'
Cc: Oleszczuk, Zachary
Subject: NDA 22-360; Nicorette mini lozenges; t-con attendees

Hi Iris,

Would you send me a list of the attendees from GSK that were at the t-con last week on 4/14/09?

The FDA attendees were:

Andrea Leonard-Segal, MD, Director DNCE
Joel Schiffenbauer, M.D., Deputy Director DNCE
Melissa Hancock Furness, Chief, Project Management Staff
Priscilla Callahan-Lyon, M.D., medical reviewer
Mary Robinson, M.S., Interdisciplinary Scientist Reviewer
Debbie Lumpkins, Interdisciplinary Scientist Team Leader
Zachary Oleszczuk, Reviewer, Division of Medication Error Prevention & Analysis
Mary Lewis, R.N., Regulatory Project Manager
Larry Bauer, R.N., M.S., Regulatory Project Manager
Cindy Li, Ph.D., Pharmacology/Toxicology Reviewer

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

4/22/2009

MEMORANDUM OF TELECON

DATE: April 14, 2009

APPLICATION NUMBER: NDA 22-360

BETWEEN:

GlaxoSmithKline

Iris H. Shelton, Assistant Director, Regulatory Affairs

David Schiffkovitz, Director, Regulatory Affairs

Erin Oliver, Director, Regulatory Affairs

Phone: 800-988-9755

AND

Office of Nonprescription Products

Leah Christl, Ph.D., Associate Director, Regulatory Affairs

Division of Nonprescription Clinical Evaluation:

Andrea Leonard-Segal, MD, Director

Joel Schiffenbauer, M.D., Deputy Director

Melissa Hancock Furness, Chief, Project Management Staff

Priscilla Callahan-Lyon, M.D., medical reviewer

Mary Lewis, R.N., Regulatory Project Manager

Larry Bauer, R.N., M.S., Regulatory Project Manager

Cindy Li, Ph.D., Pharmacology/Toxicology Reviewer

Division of Nonprescription Regulation Development:

Mary Robinson, M.S., Interdisciplinary Scientist Reviewer

Debbie Lumpkins, Interdisciplinary Scientist Team Leader

Division of Medication Error Prevention & Analysis:

Zachary Oleszczuk, PharmD, Safety Evaluator

SUBJECT: Labeling discussion

On April 14, 2009 an email transmittal was sent to GlaxoSmithKline (GSK) listing the following comments in response to GSK's February 10, 2009 submission of labeling for Nicorette Lozenge (mini), NDA 22-360. In that email we recommended that GSK make the following changes to:

Principal Display Panel:

1. The statement of identity is presented in a small size as compared to the proprietary name. We request you revise the size of the established name so that it appears in a size reasonably related to the most prominent printed matter on the principal display panel.

GSK agreed with the above.

Container Label (2 mg and 4 mg)

2. The strength on the container label is hard to see because it is embedded in the established name in a small font. Once the container is removed from the carton it is difficult to identify the strength of the product. We request you increase the size and prominence of the strength on the container label so the strength can be easily identified.

GSK agreed with the above.

Carton Side Panel

3. Under "To increase your success in quitting":
 - a. Paragraph 2. Insert the word "lozenge" after the word "mini" to complete the form descriptor.

GSK proposed to modify the statement to read: "Use enough- Use at least 9 Nicorette mini lozenges per day during the first six weeks"

The Agency agreed this was acceptable.

- b. Paragraph 3. Insert the word "lozenge" after the word "mini" to complete the form descriptor.

GSK agreed with the above.

Vial 24 and 27 count

4. Decrease the font size of the word "mini" in the form descriptor "mini lozenge". Make "mini" and "lozenge" the same size on the front of the 24 and 27 count vials.

GSK stated their belief that the presentation of the form descriptor "mini lozenge" is part of trade dress and not subject to any regulatory requirement. FDA noted that as currently presented, the form descriptor distracted from the required prominence of the statement of

identity. FDA stated there was insufficient balance in the size relationship between the brand name, statement of identity and the form descriptor. GSK agreed to take this into consideration and revise the labels by increasing the prominence of the statement of identity where ever it appears in labeling. It was agreed that the font size for "mini" and "lozenge" did not have to be identical as long as the above mentioned revisions to increase the prominence of the statement of identity were incorporated into the label.

User Guide

5. Cover page. Capitalize the letter "M" in the word "mini" in the following heading:

"How to Use Nicorette Mini Lozenges and Tips to Help you Quit Smoking".

GSK agreed with the above.

6. The word "mini" is part of the form descriptor name. Unbold the word "mini" and capitalize the "M" wherever the words "Mini Lozenges" appear in the User's Guide. Also, make the words "mini" and "lozenge" the same font and size throughout the Guide.

GSK wants to keep it the way it is and FDA agreed. See discussion in 4 above.

7. Page 3, paragraph 2, line 7: Delete the 2nd word "mini" in the paragraph. Mini is not apart of the Trade Name. Alternatively, the word "Lozenge" could be added and the word "mini" unbolded and capitalized.

GSK said that they would revise the sentence to remove the second "mini". FDA found the proposed revision acceptable.

8. Page 5, paragraph 3, bullet 1. Delete the phrase "_____". The phrase is not required according to § 201.64(c) and it is not included in the proposed "Drug Facts" carton labeling.

b(4)

GSK agreed with the above.

The t-con was held from 1:30 p.m. to 2:00 p.m.

Mary M. Lewis, RPM

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/s/

Mary Lewis
5/15/2009 03:54:20 PM
CSO

Mary Lewis
5/15/2009 03:55:05 PM
CSO

Lewis, Mary

From: Lewis, Mary
Sent: Tuesday, April 14, 2009 4:11 PM
To: 'Iris.H.Shelton@gsk.com'
Subject: RE: Re NDA 22-360 Labeling Tcon

Here they are:

Office of Nonprescription Products

Leah Christl, Ph.D.

Associate Director for Regulatory Affairs

Division of Nonprescription Clinical Evaluation:

Melissa Hancock Furness

Chief, Project Management Staff

Andrea Leonard-Segal, MD

Director

Joel Schiffenbauer, M.D., Deputy Director

Priscilla Callahan-Lyon, M.D., Medical Reviewer

Cindy Li, Ph.D., Pharmacology/Toxicology Reviewer

Mary M. Lewis, R.N., Regulatory Project Manager

Larry Bauer, R.N., M.A., Regulatory Project Manager

Division of Nonprescription Regulation Development:

Mary Robinson, M.S., Interdisciplinary Scientist Reviewer

Debbie Lumpkins, Interdisciplinary Scientist Team Leader

Division of Medication Error Prevention & Analysis (DMEPA)

Zachary Oleszcuk, Reviewer

Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Tuesday, April 14, 2009 2:24 PM
To: Lewis, Mary
Subject: Re NDA 22-360 Labeling Tcon

Hi Mary,

Thanks for arranging today's Tcon. I will draft and submit the agreements to the agency. In preparation,

4/22/2009

would appreciate if you can provide me with the list of FDA attendees.

Thanks

Iris H. Shelton

Lewis, Mary

From: Lewis, Mary
Sent: Tuesday, April 14, 2009 10:13 AM
To: 'Iris.H.Shelton@gsk.com'
Subject: NDA 22-360; Nicorette mini lozenge; label issues for today's t-con
Attachments: Label issues for tcon signed 041409.pdf

Hi Iris,

Attached is the transmittal with label issues for our 1:30 p.m. t-con today.

Please confirm you have received this email.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

4/22/2009



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products**

EMAIL TRANSMITTAL SHEET

DATE: April 14, 2009

To: Iris H. Shelton Assistant Director, Regulatory Affairs	From: Mary M. Lewis, RN Regulatory Project Manager
Company: GlaxoSmithKline	Office of Nonprescription Products
E-mail: Iris.H.Shelton@gsk.com	E-mail: Mary.1.Lewis@fda.hhs.gov
Phone number: (973) 889-2167	Phone number: (301)796-0941

Subject: NDA 22-360; Nicorette Lozenge, 2mg and 4 mg – Label issues for discussion

Total no. of pages including cover: 4

Document e-mailed: YES

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2222. Thank you.

The following comments are in response to your February 10, 2009 submission of label and labeling for Nicorette Lozenge (mini) that we recommend GlaxoSmithKline make the following changes to:

Principal Display Panel:

1. The statement of identity is presented in a small size as compared to the proprietary name. We request you revise the size of the established name so that it appears in a size reasonably related to the most prominent printed matter on the principal display panel.

Container Label (2 mg and 4 mg)

2. The strength on the container label is hard to see because it is embedded in the established name in a small font. Once the container is removed from the carton it is difficult to identify the strength of the product. We request you increase the size and prominence of the strength on the container label so the strength can be easily identified.

Carton Side Panel

3. Under "To increase your success in quitting":
 - a. Paragraph 2. Insert the word "lozenge" after the word "mini" to complete the form descriptor.
 - b. Paragraph 3. Insert the word "lozenge" after the word "mini" to complete the form descriptor.

Vial 24 and 27 count

4. Decrease the font size of the word "mini" in the form descriptor "mini lozenge". Make "mini" and "lozenge" the same size on the front of the 24 and 27 count vials.

User Guide

5. Cover page. Capitalize the letter "M" in the word "mini" in the following heading:

"How to Use Nicorette Mini Lozenges and Tips to Help you Quit Smoking".
6. The word "mini" is part of the form descriptor name. Unbold the word "mini" and capitalize the "M" wherever the words "Mini Lozenges" appear in the User's Guide. Also, make the words "mini" and "lozenge" the same font and size throughout the Guide.
7. Page 3, paragraph 2, line 7: Delete the 2nd word "mini" in the paragraph. Mini is not apart of the Trade Name. Alternatively, the word "Lozenge" could be added and the word "mini" unbolded and capitalized.

NDA 22-360

04/14/09

Page 3

8. Page 5, paragraph 3, bullet 1. Delete the phrase _____ The phrase is not required according to § 201.64(c) and it is not included in the proposed "Drug Facts" carton labeling.

b(4)

Carton Side Panel Question for Clarification:

Side Panel bottom. The offline support program is "www.nicorette.com, but in the User's Guide the support program is given as www.committedquitters.com. Are they the same or different programs?

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this page is the manifestation of the electronic signature.**

/s/

Mary Lewis
4/14/2009 10:07:56 AM
CSO

Lewis, Mary

From: Lewis, Mary
Sent: Monday, April 13, 2009 4:49 PM
To: 'Iris.H.Shelton@gsk.com'
Subject: NDA 22-360; Nicorette mini lozenge; issues for the t-con

Hi, Iris,

I will have to send you the issues tomorrow, morning I hope. We are still working on the wording.

My apologies.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

4/22/2009

Lewis, Mary

From: Lewis, Mary
Sent: Monday, April 13, 2009 12:01 PM
To: 'Iris.H.Shelton@gsk.com'
Subject: RE: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Iris,

The call in number is:
1-800-988-9755
passcode: 49213

I hope to email you the issues sometime this afternoon.

Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Monday, April 13, 2009 8:19 AM
To: Lewis, Mary
Subject: RE: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Mary,
That time will work for our team. Greatly appreciate if you could provide us with some of the issues that will be discussed, as well as a call in number.
Thanks
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

10-Apr-2009 18:21

To Iris.H.Shelton@gsk.com

cc "Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

Subject RE: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Iris,

We've had some conflicts in the schedule and we need to change the t-con to Tuesday, 4/14/09 from 1:30 to 2 p.m. Please let me know if that works for your team.

Thank you.

Mary

4/22/2009

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Friday, April 10, 2009 8:33 AM
To: Lewis, Mary
Subject: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Mary,
This is in reference to the Tcon for NDA 22-360. Appreciate if you could provide us with a call in number.
Thanks
Iris
GlaxoSmithKline Consumer Healthcare

4/22/2009

Lewis, Mary

From: Lewis, Mary
Sent: Friday, April 10, 2009 4:22 PM
To: 'Iris.H.Shelton@gsk.com'
Cc: Lewis, Mary
Subject: RE: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Iris,

We've had some conflicts in the schedule and we need to change the t-con to Tuesday, 4/14/09 from 1:30 to 2 p.m. Please let me know if that works for your team.

Thank you.

Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Friday, April 10, 2009 8:33 AM
To: Lewis, Mary
Subject: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Mary,

This is in reference to the Tcon for NDA 22-360. Appreciate if you could provide us with a call in number.

Thanks

Iris

GlaxoSmithKline Consumer Healthcare

4/22/2009

Lewis, Mary

From: Lewis, Mary
Sent: Monday, April 06, 2009 11:29 AM
To: 'Iris.H.Shelton@gsk.com'
Cc: Lewis, Mary
Subject: NDA 22-360; Nicorette Lozenge; t-con for label discussion

Hi Iris,

We would like to have a t-con with GSK to discuss the label for Nicorette lozenge on Monday, 4/13/09 from 10:00 to 11:00 a.m. EST.

Let me know if that works for you.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

4/22/2009

Lewis, Mary

From: Lewis, Mary
Sent: Friday, April 03, 2009 2:12 PM
To: 'Iris.H.Shelton@gsk.com'
Cc: Lewis, Mary
Subject: RE: Message from 9738892100; NDA 22-360

Follow Up Flag: Follow up
Flag Status: Red

Hi Iris,

I received your phone message. With regard to NDA 22-360 and the 81 count it shouldn't have an affect on the PDUFA. What I don't know is what the action will be until a later time.

Mary.

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941

—Original Message—

From: Unity Messaging System - FDAVOIP14
Sent: Friday, April 03, 2009 12:45 PM
To: Lewis, Mary
Subject: Message from 9738892100

<< File: VoiceMessage >>



NDA 22-360

INFORMATION REQUEST LETTER

GlaxoSmithKline Consumer Healthcare, L.P.
Attention: Iris H. Shelton
Assistant Director, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Ms. Shelton:

Please refer to your July 18, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nicorette Lozenge (nicotine polacrilex) 2 mg and 4 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following information requests. We request a prompt written response in order to continue our evaluation of your NDA.

In the stability section 3.2.P.8.1, there are two conflicting statements regarding the storage temperatures. Please revise _____ to "store at 20 - 25 °C".

b(4)

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Mary Lewis, Regulatory Project Manager the Office of New Drugs (Mary.l.Lewis@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Moo-Jhong Rhee
4/1/2009 02:12:32 PM
Chief, Branch III

Lewis, Mary

From: Lewis, Mary
Sent: Friday, March 27, 2009 1:42 PM
To: 'Iris.H.Shelton@gsk.com'
Subject: NDA 22-360

Hi Iris,

Your question regarding the 81 count pack is under discussion. We will not have a response for you until early next week and I wanted you to know that as soon as I realized it.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Thursday, March 26, 2009 3:28 PM
To: Lewis, Mary
Subject: Re: NDA 22-360; Nicorette lozenge (mini); clarification
Importance: High

Hi Mary,

In the submission, we included a vial count size of 24 and 27 lozenges. The original submission provided for SKUS for 24 _____ and 108 count sizes. Currently GSK is considering launching the product in the 24 count as well as an SKU of 81 count lozenges (3 vials of 27) only. The 81 count size was not included in the original submission and we would like to ensure that introduction of this new SKU would not impact the PDUFA timings of the submission. Thank you.

b(4)

Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

26-Mar-2009 14:58

To: Iris.H.Shelton@gsk.com
cc
Subject: NDA 22-360; Nicorette lozenge (mini); clarification

Hi Iris,

Please email me your questions so I can have the proper team members respond.

Let me know what you have submitted and what your Brand Managers want to submit.

Thanks.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

4/22/2009



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-360

INFORMATION REQUEST LETTER

GlaxoSmithKline
Attention: Iris H. Shelton
Assistant Director, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Ms. Shelton:

Please refer to your July 18, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nicorette Lozenge (2 mg and 4 mg, nicotine polacrifex).

We are reviewing the Chemistry, Manufacturing and Controls and proprietary names sections of your submission and have the following revision and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- Revise the acceptance criteria of the Appearance test (Table 1 in Section 3.2.P.7) for the container/closure system as follows: _____

- There is no stability information in section 3.2.P.8.3 of your application to support your statement in 3.2.P.8.1, "_____". Please clarify the two different storage temperature statements in your product label (*Store at 20 - 25°C (68 - 77°F)*) and in the section 3.2.P.8.1 _____
- In an email dated January 9, 2009, you proposed to use the proprietary name Nicorette for NDA 22-360 and all of the currently marketed Commit Lozenge products. Please state your transition plan for the currently marketed Commit lozenges to Nicorette.

b(4)

b(4)

- **It is our understanding that GSK intends to use distinct callouts to differentiate between the products in the Nicorette product line (i.e. lozenges, gum etc.). Please provide representative labels of the primary display panels for the currently marketed Nicorette products for comparison of the proposed carton labeling for NDA 22-360.**

If you have any questions, call Mary Lewis, Regulatory Health Project Manager, at 301-796-0941.

Sincerely,

{See appended electronic signature page}

**Andrea Leonard Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research**

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this page is the manifestation of the electronic signature.**

/s/

Andrea Segal

3/11/2009 04:42:22 PM

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 24, 2009

TO: Andrea Leonard Segal, MD
Director
Division of Nonprescription Clinical Evaluation
(DNCE)

FROM: Xikui Chen, Ph.D.
Division of Scientific Investigations

THROUGH: C.T. Viswanathan, Ph.D. *Wart - K. Yan 2/24/2009*
Associate Director - Bioequivalence
Division of Scientific Investigations

SUBJECT: Review of EIR Covering NDA 22-360, Commit[®]
(Nicotine) 2 mg and 4 mg Mini Lozenges, Sponsored
by GlaxoSmithKline

At the request of DNCE, the Division of Scientific Investigations conducted audits of the clinical and analytical portions of the following bioequivalence study:

Study S3010567: A Single Dose Bioequivalence Study of 2 mg and 4 mg Mini Nicotine Lozenges

-Both the clinical and analytical portions of the study were conducted at MDS Pharma Services, Lincoln, NE (MDS-SPS). Following the inspection (12/8-11/08), Form FDA-483 was issued (Attachment 1). Our evaluation of the significant findings and sponsor's response to the Form FDA-483 (Clinical Report Addendum dated February 6, 2009), are as follows:

Clinical Site: MDS Pharma Services, Lincoln, NE

No significant findings were observed.

Analytical Site: MDS Pharma Services, Lincoln, NE

1. The quality control (QC) samples (3.00, 30.0 and 150 ng/ml) and calibration range (1.00 to 200 ng/ml) for nicotine used in the study AA72584-01 (protocol S3010567)

were not representative of the nicotine plasma concentrations observed in study plasma samples. For example, the mean peak nicotine concentrations (C_{max}) following dosing of 2 mg and 4 mg lozenges were 4.3 to 4.5 ng/ml, and 6.7 to 7.7 ng/ml, respectively. These mean C_{max} values were much lower than the mid QC value (30 ng/ml).

In response to the FDA 483 observations, MDSPS reanalyzed all the study plasma samples collected in the 2 mg and 4 mg nicotine lozenges studies. In the reanalysis, quality control samples at concentrations of 0.60, 3.00 and 7.50 ng/mL, and calibration range of 0.20 ng/mL to 10.0 ng/mL were utilized. The QC samples and calibration curve range used in the reassay (December 19, 2008 to January 6, 2009), were found to be representative of the plasma nicotine concentrations generated in the studies.

2. The LC/MS/MS assay (LLOQ = 1.00 ng/ml) does not have sufficient sensitivity to measure nicotine levels for at least three half lives in the study of 2 mg lozenges. The total AUC (AUC_{0-inf}) values included a large extrapolated component. For example: the ratio of AUC_{0-t}/AUC_{0-inf} was 0.73 for test group, and 0.75 for reference group.

Upon the request of the sponsor, MDSPS reanalyzed all the study samples from the 2 mg and 4 mg nicotine lozenges study using 0.20 ng/ml as the lower limited of quantitation (LLOQ). The LLOQ at 0.2 ng/mL was validated and the supporting data are provided in Amendment 2 of the Validation Report. This LC/MS/MS assay (LLOQ = 0.20 ng/ml) was able to measure nicotine levels for more than three half lives in both the 2 mg and 4 mg nicotine lozenges studies. Please note that the study plasma samples were stored at -20 °C for 10 months prior to the reanalysis performed in December 2008. A review of stability data in Validation Amendment 2 showed that plasma samples were stable for 521 days when stored at -20 °C.

Conclusion:

Following our evaluation of the inspectional findings and the response, DSI is of the opinion that MDSPS has adequately addressed the Form FDA-483 Observations, and we

Page 3 of 3 - NDA 22-360, Commit® (Nicotine) 2 mg and 4 mg
Mini Lozenges

recommend that the clinical and analytical data of Study
S3010567 be accepted for review.

After you have reviewed this transmittal memo, please
append it to the original NDA submission.

Xikui Chen, Ph.D.

Final Classification:

VAI - MDS Pharma Services, Lincoln, NE

CC:

DSI/Vaccari

DSI/Viswanathan/Chen/Martin Yau

DSI/Patague/Rivera-Lopez/CF

OND/ONP/DNCE/Mary Lewis

OTS/OCF/DCP2/Doddapaneni/Ping Ji

HR-SW3515/Ismael Olvera

HR-SW350/Carl Montgomery

Draft: XC 12/30/08; 2/19/09

Edit: JAO 1/5/09; MKY 2/19/09

DSI: 5900; O:\BE\eircover\22360gla.nic.doc

FACTS: 978500

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this page is the manifestation of the electronic signature.**

/s/

Xikui Chen

2/25/2009 10:47:09 AM

COMPLIANCE OFFICER

Dr. Yau (Acting for Dr. Viswanathan); Hard copies available
upon request.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION			
DISTRICT OFFICE ADDRESS AND PHONE NUMBER Food & Drug Administration 11630 W. 80 th St. Lenexa, KS 66214		DATE(S) OF INSPECTION 12/8 - 11/2008	
(913) 752-2100		FEI NUMBER 1915582	
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED To: Gary H. Diesel, Clinical Site Director			
FIRM NAME MDS Pharma Services		STREET ADDRESS 621 Rose Street	
CITY, STATE AND ZIP CODE Lincoln, NE 68502		TYPE OF ESTABLISHMENT INSPECTED Analytical Research Facility/Biopharmaceutical Clinic	
DURING AN INSPECTION OF YOUR FIRM I OBSERVED: THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.			
<p>1) THE QUALITY CONTROL (QC) SAMPLES (3.00, 30.0 AND 150 ng/mL) AND CALIBRATION RANGE (1.00 TO 200 ng/mL) FOR NICOTINE USED IN THE STUDY RA 72504-01 (PROTOCOL 33010567) WERE NOT REPRESENTATIVE OF THE NICOTINE PLASMA CONCENTRATIONS OBSERVED IN STUDY PLASMA SAMPLES. FOR EXAMPLE, THE MEAN PERAL NICOTINE CONCENTRATIONS (C_{max}) FOLLOWING DOSING OF 2 mg AND 4 mg LOZENGES WERE 4.3 TO 4.5 ng/mL, AND 6.7 TO 7.7 ng/mL, RESPECTIVELY. THESE MEAN C_{max} VALUES WERE MUCH LOWER THAN THE MID QC VALUE (30 ng/mL).</p> <p>2) THE LC/MS/MS ASSAY (LLOQ = 1.00 ng/mL) DOES NOT HAVE SUFFICIENT SENSITIVITY TO MEASURE NICOTINE LEVELS FOR AT LEAST THREE HALF LIVES IN THE STUDY OF 2 mg LOZENGES. THE TOTAL AUC ($AUC_{0-\infty}$) VALUES INCLUDED A LARGE EXTRAPOLATED COMPONENT. FOR EXAMPLE, THE RATIO OF $AUC_{0-t} / AUC_{0-\infty}$ WAS 0.73 FOR TEST GROUP, AND 0.75 FOR REFERENCE GROUP.</p>			
SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE <i>J. Diesel</i> <i>Z. Khan</i>	EMPLOYEE(S) NAME AND TITLE Gary H. Diesel, Clinical Site Director, Investigator, Ismael Ojeda, Chemist <i>Xi Hua Chen</i>	DATE ISSUED 12/11/2008

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Thursday, February 19, 2009 1:21 PM
To: Lewis, Mary
Subject: Re: NDA 22-360; Nicorette mini lozenges; dataset request
Follow Up Flag: Follow up
Due By: Thursday, February 19, 2009 4:00 PM
Flag Status: Red

Hi Mary,

We were able to reply to your request today and the submission has been sent in. Please let me know if you need any additional information.

Regards,

Iris

3/10/2009

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Thursday, February 19, 2009 10:54 AM
To: Lewis, Mary
Subject: Re: NDA 22-360; Nicorette mini lozenges; dataset request

Hi Mary,
We will aim to submit this to you tomorrow.
Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

19-Feb-2009 09:20

To Iris.H.Shelton@gsk.com
cc
Subject NDA 22-360; Nicorette mini lozenges; dataset request

Hi Iris,

We noticed that you submitted the BE study data listings in pdf format. Please provide the PK concentration profile datasets in SAS transport file format (*.xpt) (both actual sampling times and nominal sampling times are needed). In addition, provide the derived PK parameter datasets used for BE analysis in SAS file format.

We would appreciate this information as soon as possible.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Tuesday, February 17, 2009 9:43 AM
To: Lewis, Mary
Subject: Re: NDA 22-360; Nicorette mini lozenge; DMF issue

Hi Mary,
I will look into this and get back to you.
Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

13-Feb-2009 15:37

To Iris.H.Shelton@gsk.com

cc

Subject NDA 22-360; Nicorette mini lozenge; DMF issue

Hi Iris,

FYI: There were two separate information request letters sent to the DMF holder. The DMF response of 1/15/09 answers one issue, but we sent them another letter on January 23, 2009 that we have not received a response to.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Wednesday, February 11, 2009 4:27 PM
To: Lewis, Mary
Subject: Re: NDA 22-360; Nicorette lozenge;

Hi Mary,
I'm in the process of obtaining the information, and am targetting to have a formal response to you by the end of this week.
Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

11-Feb-2009 15:19

To Iris.H.Shelton@gsk.com
cc
Subject NDA 22-360; Nicorette lozenge;

Hi Iris,

In the information request letter that we sent you dated 1/29/09 I received your response of 2/10/09 and 2/11/09. In these letters you responded to the first issue, number 1. When can we look for responses to issues #2 through #4?

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

[attachment "IR letter emailed tradename DMF container 012909. pdf.pdf" deleted by Iris H Shelton/PAR/CH/SB_PLC]

3/10/2009

Lewis, Mary

From: Lewis, Mary
Sent: Friday, February 06, 2009 9:13 AM
To: 'Iris.H.Shelton@gsk.com'
Subject: RE: NDA 22-360; Commit mini lozenge; your 2 phone calls

OK. We are on for 12:30 p.m. I can call you. Is 973-889-2167 the correct number to call?

THanks.
Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Thursday, February 05, 2009 4:44 PM
To: Lewis, Mary
Subject: Re: NDA 22-360; Commit mini lozenge; your 2 phone calls

Hi Mary,
It certainly works. Thanks
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

05-Feb-2009 16:27

To Iris.H.Shelton@gsk.com

cc

Subject NDA 22-360; Commit mini lozenge; your 2 phone calls

Hi Iris,

In response to your phone message I'm trying to set up a t-con for 12:30 to 1 p.m. tomorrow, 2/6/09. I'm waiting to hear back from the tradename reviewer to confirm this time works for him.

Will this time work for you.

Thanks.

Mary

3/10/2009

Lewis, Mary

From: Lewis, Mary
Sent: Wednesday, February 04, 2009 3:12 PM
To: 'Iris.H.Shelton@gsk.com'
Cc: Lewis, Mary
Subject: NDA 22-360; Commit Mini Lozenge; request for information

Hi Iris,

On 1/13/09 GSK sent us the PDP with Nicorette mini lozenge, 2 mg and 4 mg for _____ package.

b(4)

We would like to see labeling for each SKU to be marketed for review. Also, please send us a sample of "Drug Facts" for the Nicorette mini lozenge. We are trying to review this and we only have Drug Facts for Commit mini lozenge from the July, 2008 submission.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-360

INFORMATION REQUEST LETTER

GlaxoSmithKline Consumer Healthcare, L.P.
Attention: Iris H. Shelton
Assistant Director, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Ms. Shelton:

Please refer to your July 18, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Commit Mini Lozenges (nicotine polacrilex) 2 mg and 4 mg.

We are reviewing the Chemistry, Manufacturing and Controls, labeling and proprietary name sections of your submission and have the following information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. We would like to ensure that we have a trade name for this product prior to completing the NDA process. We request that you submit the proprietary name you plan to use for this product. Please send it as an amendment to NDA 22-360. If you choose to use the trade name "Nicorette" for this product, you will need to withdraw the name "Commit" from this NDA.
2. We have identified a deficiency with DMF _____ This information has been communicated to the DMF holder. b(4)
3. The following issues/request for information have been identified regarding your drug product's container closure system:
 - Provide a diagram and indicate where the _____ is integrated in the container/closure system. Add an attribute and specification to ensure that this feature is not compromised upon receipt of the container/closure. b(4)
 - For appropriate and complete review of the container/closure system, specify the relevant information in DMF _____, including the product code number and the specifications, for the container/closure system. b(4)
 - Submit the suppliers' CoAs for the container/closure system and for the _____

- Provide detailed information for the _____ (vial) with _____ mentioned in Section 3.2.P.8.1 *Stability summary and Conclusion*. If the vial is different from the proposed to-be-marked container/closure system:
 - 1) provide a comparison for the two systems for critical properties, fabrication materials and suppliers, and
 - 2) provide a table which describes the container/closure systems used in the registration stability study for each lot of the drug product in the study.

b(4)

4. We are concerned with the following statement on your carton label: _____
_____. Please clarify the nature and the source of the _____ and explain why the _____

b(4)

If you have any questions, call Mary Lewis, Regulatory Health Project Manager, at 301-796-0941.

Sincerely,

{See appended electronic signature page}

Melissa Furness
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Melissa Furness
1/29/2009 11:46:55 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Office of New Drugs - Immediate Office
Pediatric and Maternal Health Staff
Silver Spring, MD 20993
Telephone 301-796-2200
FAX 301-796-9855

M E M O R A N D U M

Date: January 26, 2009

From: Amy M. Taylor, MD, MHS, Medical Officer
Pediatric and Maternal Health Staff

Through: Hari Cheryl Sachs, MD, Team Leader
Pediatric and Maternal Health Staff, Office of New Drugs

Lisa Mathis, MD, OND Associate Director
Pediatric and Maternal Health Staff, Office of New Drugs

To: Andrea Leonard-Segal, MD, MS, Director
Division of Nonprescription Clinical Evaluation

Re: Studies required under PREA for Commit[®] (nicotine polacrilex) Mini[™] Mint Lozenge

Document ID Number: NDA 22-360 CDER Stamp Date: 7/18/08

Sponsor: GlaxoSmithKline Consumer Health, L.P.

Drug: Commit[®] (nicotine polacrilex) Mini[™] Mint Lozenge

Indication: Reduces withdrawal symptoms, including nicotine craving, associated with quitting smoking.

Dosage form and route of administration: 2 mg and 4 mg oral lozenge

Dosing regimen: Weeks 1 to 6, one lozenge every 1 to 2 hours
Weeks 7 to 9, one lozenge every 2 to 4 hours

Weeks 10 to 12, one lozenge every 4 to 8 hours

If you smoke your first cigarette within 30 minutes of waking up in the morning, use 4 mg nicotine lozenges.

If you smoke your first cigarette more than 30 minutes after waking up in the morning, use 2 mg nicotine lozenges.

Consult Question:

The Division of Nonprescription Clinical Evaluation (DNCE) requests that PMHS review the Sponsor's waiver and deferral requests and comment on required pediatric studies.

Background

This original NDA was submitted for review on July 18, 2008. The NDA was accepted for filing on September 29, 2008 and the PDUFA goal date is May 18, 2008. The Sponsor is seeking approval to market a smaller version of Commit[®] Nicotine Polacrilex Lozenge, 2 mg and 4 mg.

Commit[®] Nicotine Polacrilex Lozenge, NDA 21-330, (not the mini lozenge) was originally approved in adults to be marketed as an over-the-counter product on October 31, 2002. Labeling for pediatric patients states: "If you are under 18 years of age, ask a doctor before use." The approval letter included a postmarketing requirement (PMR) to which the Pediatric Research Equity Act (PREA) 2003 applied. The PMR stated:

For the marketing of Commit[™] (nicotine polacrilex lozenge), to reduce withdrawal symptoms, including nicotine craving, associated with quitting smoking, we are deferring submission of pediatric studies for patients 10-17 years until October 31, 2007. We are waiving the pediatric study requirement for this application for patients under age 10.

In August 2007, the Sponsor submitted a clinical study report of a pharmacokinetic and safety study of nicotine replacement therapies in adolescent smokers. The study was originally designed to evaluate the NPA nicotine lozenge, NicoDerm CQ Nicotine Transdermal Patch, Nicorette Nicotine Gum, and the Nicorette sublingual tablet. However, the Nicorette sublingual tablet was not evaluated in this study after a business decision was made not to investigate the sublingual tablet.

In April 2008, the Division of Nonprescription Clinical Evaluation (DNCE) issued a response to the submitted study stating that terms of the PMR were not met since the PK study submitted did not adequately assess the safety and efficacy of Commit[™] in children ages 10-17 years. The Sponsor has requested a meeting to discuss the Division's letter.

Request for Waiver and Deferral of Pediatric Studies

The Sponsor requests a waiver of studies of Commit[®] (nicotine polacrilex) Mini[™] Mint Lozenge for pediatric patients ages 0 to 10 years. The justification given for the waiver is

that the age range represents a small population with significant nicotine dependence. Nicotine replacement therapy does not represent a meaningful therapeutic benefit and is not likely to be used by a substantial number of pediatric patients in that age group. The Sponsor further states that this population tends to have direct parental supervision and lacks the financial means to purchase the product.

The Sponsor requests a deferral of pediatric studies of Commit[®] (nicotine polacrilex) Mini[™] Mint Lozenge in patients ages ≥ 10 to 17 years. The Sponsor states that reason for the request is that the PK study of the NPA nicotine lozenge, NicoDerm CQ Nicotine Transdermal Patch, and Nicorette Nicotine Gum submitted to the FDA in August 2007 was still under review and the study could cover similar issues in the new formulation (Commit[®] Mini[™] Mint Lozenges).

Response to Division's Consult Question

PREA does not apply to this application and no studies in pediatric patients are required. A waiver or deferral is unnecessary. PREA requires pediatric studies for any application or supplement submitted under section 505 with a new active ingredient, indication, dosing regimen, dosage form or route of administration. The active ingredient, indication, dosing regimen and route of administration are exactly the same in this NDA as the approved product Commit[®] Nicotine Polacrilex Lozenge (NDA 21-330). During an internal meeting with the division review team on December 12, 2008, the division review team confirmed that the mini lozenge does not represent a new dosage form. The PMR for Commit[®] Nicotine Polacrilex Lozenge remains.

Reviewer's comment: NDA 22-360 does not trigger PREA. The following point is made only in reference to applications for other products that may be submitted in the future. The legislative criteria for a waiver are:

- a. Studies are impossible or highly impractical (e.g. the number of pediatric patients is so small or is geographically dispersed;*
- b. The product would be ineffective or unsafe in one or more of the pediatric group(s) for which a waiver is being requested;*
- c. The product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is unlikely to be used in a substantial number of all pediatric age groups or the pediatric age group(s) for which a waiver is being requested; or*
- d. Reasonable attempts to produce a pediatric formulation for one or more of the pediatric age group(s) for which the waiver is being requested have failed. (Provide documentation from Sponsor).*

PREA does not allow for waiving required studies based on the financial means of the intended population. Waiving studies in pediatric patients under 10 years of age is consistent with regulatory actions on similar products, but the supporting criteria should be that the necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed) rather than that the product does not represent a meaningful therapeutic benefit and is not likely to be used in a substantial number of patients.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Amy M. Taylor
1/26/2009 03:40:47 PM
MEDICAL OFFICER

Hari Sachs
1/27/2009 12:40:01 PM
MEDICAL OFFICER

Lisa Mathis
1/28/2009 08:33:10 PM
MEDICAL OFFICER

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Friday, January 09, 2009 11:57 AM
To: Lewis, Mary
Subject: RE: NDA 22-360; Commit mini lozenge; IR letters

Hi Mary

GSK is considering marketing all of the lozenges (including the currently marketed Commit) under the "Nicorette" tradename. There will be distinct callouts for gum, lozenge and mini lozenges. I'm just waiting for the front panel with callouts and then will submit formally.

Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

09-Jan-2009 10:21

To Iris.H.Shelton@gsk.com
cc
Subject RE: NDA 22-360; Commit mini lozenge; IR letters

Hi Iris,

Thanks for your response. Would it be possible to tell us the proposed name by Monday, 1/12/09?

Thanks.

Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Friday, January 09, 2009 9:03 AM
To: Lewis, Mary
Subject: Re: NDA 22-360; Commit mini lozenge; IR letters

Hi Mary,

I'm working on the 12/15 letter and will try to have it to you early next week, will try for the 12th.. With respect to the chemistry letter, the team has met and is reviewing data, having just returned from shutdown.. We are meeting on the 13th at which time I will have a better sense of timing. Also with respect to the vials, how many would you like to receive? I will be sending them directly to you.

Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

08-Jan-2009 16:45

To Iris.H.Shelton@gsk.com
cc

3/10/2009

Subject NDA 22-380; Commit mini lozenge; IR letters

Hi Iris,

Happy New Year to you too!

Can you tell me the status of GSK responding to our information request letters of 12/15/08 and chemistry's information request letter of 12/19/09?

Is there anyway we could receive responses by close of business Monday, 1/12/09?

Thanks.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009

Lewis, Mary

From: Lewis, Mary
Sent: Friday, January 09, 2009 10:21 AM
To: 'Iris.H.Shelton@gsk.com'
Subject: RE: NDA 22-360; Commit mini lozenge; IR letters

Hi Iris,

Thanks for your response. Would it be possible to tell us the proposed name by Monday, 1/12/09?

Thanks.

Mary

From: Iris.H.Shelton@gsk.com [mailto:Iris.H.Shelton@gsk.com]
Sent: Friday, January 09, 2009 9:03 AM
To: Lewis, Mary
Subject: Re: NDA 22-360; Commit mini lozenge; IR letters

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Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

08-Jan-2009 16:45

To Iris.H.Shelton@gsk.com

cc

Subject NDA 22-360; Commit mini lozenge; IR letters

Hi Iris,

Happy New Year to you too!

Can you tell me the status of GSK responding to our information request letters of 12/15/08 and chemistry's information request letter of 12/19/09?

Is there anyway we could receive responses by close of business Monday, 1/12/09?

Thanks.

3/10/2009

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Wednesday, January 07, 2009 10:29 AM
To: Lewis, Mary
Subject: Re: NDA 22-360; Request for Information
Follow Up Flag: Follow up
Flag Status: Red
Attachments: Response to FDA tolerability question Jan 09.doc

Hi Mary,
Happy New Year!. Attached please find our response to the inquiry noted below. Please let me know if you need any additional information. Thanks.

Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

22-Dec-2008 14:52

To Iris.H.Shelton@gsk.com
cc
Subject NDA 22-360; Request for Information

Hi Iris,

Does GSK have any additional data regarding oral safety of the mini lozenge, particularly any physical examination of the mouth or oral cavity after using the lozenges that shows no significant irritation? If you do, could you provide it to us as soon as possible?

Please confirm you have received this email.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899

3/10/2009

Email: Mary.I.Lewis@fda.hhs.gov

3/10/2009

January 7, 2009

Dear Mary,

The FDA's question/request for information on the oral tolerance of the Mini Mint lozenge was originally addressed in "The Response to FDA Question 2: Information regarding the local safety of the mini lozenge in the mouth" and was included with the submission of the Integrated Summary of Safety on October 3, 2008. GSKCH has no additional oral tolerability data to report on since the issuance of this document.

Although the oral tolerance of the Mini Mint lozenge was not specifically evaluated as a clinical end-point in the three submission studies (S3010567, S3010445, and S3010466), Adverse Events (AE's) across body systems including the mouth and throat were spontaneously captured. Review of pooled AE's from the three submission studies show relatively few incidences of events related to the mouth or throat. There is only one report of pharyngolaryngeal pain for both the 4mg Mini Mint lozenge and 4mg Commit and one report of tongue eruption for 4mg Commit. In addition to the similar oral AE profiles elicited by the two product forms, all three submission studies demonstrated bioequivalent levels of nicotine delivery between the Mini Mint lozenge and the marketed Commit lozenge.

In summary, our position on the local tolerability of the Mini Mint lozenge being similar to the marketed Commit lozenge is based on 1) bioequivalent levels of nicotine delivery between the Mini Mint lozenge and the marketed Commit lozenge, 2) similar adverse event (AE) profiles between the Mini Mint lozenge and the marketed Commit lozenge, and 3) the way in which the Mini Mint lozenge is intended to be used (moved around the mouth until dissolution). Information related to bioequivalence and safety is based upon submission studies S3010567, S3010445, and S3010466. It should be noted that AE's were spontaneously collected in all three trials.

Taken together, these observations, combined with the way in which the Mini Mint lozenge is intended to be used (moved around the mouth until dissolution similar to how the currently marketed Commit Lozenge is used), provide sufficient support for the oral tolerance and safety of the Mini Mint lozenge.

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Monday, December 22, 2008 3:26 PM
To: Lewis, Mary
Cc: David, Jeannie C
Subject: NDA 22-360 FDA Request for Information
Attachments: Scan001.PDF

Mary,
This document was just submitted to the subject NDA. We will try and address all the issues promptly in light of the holiday shutdown at GSK.

—

Regards,
Iris

3/10/2009



GlaxoSmithKline

December 22, 2008

Dr. Andrea Leonard-Segal
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Food and Drug Administration
Center for Drug Evaluation and Research
5901-Ammendale Road
Beltsville, MD 20705-1266

GlaxoSmithKline
1500 Littleton Road
Parlissary, NJ
07054-3884

Tel. 973 889 2100
Fax. 973 889 2390
www.gsk.com

Re: NDA 22-360
Commit®(nicotine polacrifex) Mini Mint 2mg and 4mg Lozenge

Dear Dr. Leonard-Segal,

Reference is made to GlaxoSmithKline's (GSK) New Drug Application (NDA 22-360) for new Commit® (nicotine polacrifex) Mini Mint Lozenges 2mg and 4mg. Reference is also made your letters of December 15, 2008 and December 19, 2008 requesting additional information pertaining to this application. Please be advised that we are reviewing the items and intend to amend the application to address your concerns.

If you have any questions, or require additional information, please contact me at (973)-889-2167.

Sincerely,

Iris H. Shelton
Assistant Director, Regulatory Affairs
GlaxoSmithKline Consumer Healthcare

Attachments for FDA Form 356h - nicotine polacrilex lozenge 2 mg & 4 mg

Chemical Name:

2 propenoic acid, 2-methyl-polymer with diethenylbenzene, complex with (S)-3-(1-methyl-2-pyrrolidinyl) pyridine

Establishment Information:

Drug Substance Manufacturer (nicotine polacrilex)

Name: GlaxoSmithKline Pharmaceuticals
Address: Shewalton Road
Irvine
Ayrshire, KA11 5AP
Scotland, UK
Contact: Alan Gray
Quality Assurance Manager
Telephone No.: 011 44 1294 847136
Registration No.: FC UK 684
DMF No.: N/A
Manufacture Steps/Type of testing performed at site: All aspects of drug substance manufacture, testing and packaging
Ready for Inspection: Yes

Drug Product Manufacturer:

Name: GlaxoSmithKline Consumer Healthcare
Address: Verenes Industrial Park
65 Windham Blvd.
Aiken, South Carolina
29805
Contact: Teresa Shumaker
Quality Assurance Director
Telephone No.: 803-642-6105
Registration No.: 1046838/ATL
DMF No.: N/A

**Manufacture Steps/Type of
testing performed at site:**

**All aspects of drug
product manufacture,
testing and packaging**

Ready for Inspection:

Yes

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Chesapeake Consumer Healthcare, L.P.		DATE OF SUBMISSION 12/22/2008	
TELEPHONE NO. (Include Area Code) 873-888-2167		FACSIMILE (FAX) Number (include Area Code) 973-888-2244	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 1500 Littleton Road Parlappany, NJ 07054-3884		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Not Applicable	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued)		INDA 22-380
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Nicotine Polacrifin	PROPRIETARY NAME (trade name) IF ANY Commit Mini Lozenges	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any)	CODE NAME (if any)	
DOSEAGE FORM Lozenges	STRENGTHS 2mg and 4mg	ROUTE OF ADMINISTRATION oral
(PROPOSED) INDICATION(S) FOR USE: reduction of withdrawal symptoms, including nicotine craving associated with quitting smoking		

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)	
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 205 (b)(1) <input type="checkbox"/> 205 (b)(2)	
IF AN ANDA, OR 205(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____	
TYPE OF SUBMISSION (check one) <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input checked="" type="checkbox"/> OTHER (General Correspondence)	
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____	
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)	
REASON FOR SUBMISSION General Correspondence- Response to FDA request for information	

PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS <input type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input checked="" type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFR), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See attached:

Cross References (List related License Applications, NDAs, NDAs, PMAs, 510(k)s, IDEs, DMFs, and DMF's referenced in the current application)
IND 58,295, NDA 21-330, DMF _____, DMF _____, DMF _____, DMF _____

b(4)

This application contains the following items: (Check all that apply)		
<input checked="" type="checkbox"/>	1. Index	
<input checked="" type="checkbox"/>	2. Labeling (check one)	<input checked="" type="checkbox"/> Draft Labeling <input checked="" type="checkbox"/> Final Printed Labeling
<input checked="" type="checkbox"/>	3. Summary (21 CFR 314.50 (c))	
<input checked="" type="checkbox"/>	4. Chemistry section	
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)	
<input checked="" type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))	
<input checked="" type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(v)(b); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)	
<input checked="" type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))	
<input checked="" type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (i)(2)(A))	
<input checked="" type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)	
<input checked="" type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))	
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (f)(3))	
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)	
<input checked="" type="checkbox"/>	19. Financial Information (21 CFR Part 54)	
<input checked="" type="checkbox"/>	20. OTHER (Specify)	
CERTIFICATION		
<p>I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:</p> <ol style="list-style-type: none"> 1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 620. 2. Biological establishment standards in 21 CFR Part 600. 3. Labeling regulations in 21 CFR Parts 201, 608, 610, 680, and/or 808. 4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202. 5. Regulations on making changes in application in FD&C Act section 508A, 21 CFR 314.71, 314.72, 314.97, 314.98, and 601.12. 6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81. 7. Local, state and Federal environmental impact laws. <p>If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.</p> <p>The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.</p> <p>Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.</p>		
SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT		TYPED NAME AND TITLE
Iris H. Shelton		Iris H. Shelton, Assistant Director, Regulatory Affairs
DATE:		12/22/2008
ADDRESS (Street, City, State, and ZIP Code)		Telephone Number
1800 Littleton Road, Parsippany, NJ 07054-3884		873-589-2167
<p>Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p>		
Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research Central Document Room 8001-S Annapolis Road Beltsville, MD 20705-1208	Department of Health and Human Services Food and Drug Administration Center for Biological Evaluation and Research (HFM-89) 1401 Rockville Plaza Rockville, MD 20852-1448	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Lewis, Mary

From: Iris.H.Shelton@gsk.com
Sent: Monday, December 22, 2008 2:54 PM
To: Lewis, Mary
Subject: Re: NDA 22-360; Request for Information

Hi Mary,
This is to confirm receipt. I'll forward this request to the team to address.
Regards,
Iris

"Lewis, Mary" <Mary.1.Lewis@fda.hhs.gov>

22-Dec-2008 14:52

To Iris.H.Shelton@gsk.com
cc
Subject NDA 22-360; Request for Information

Hi Iris,

Does GSK have any additional data regarding oral safety of the mini lozenge, particularly any physical examination of the mouth or oral cavity after using the lozenges that shows no significant irritation? If you do, could you provide it to us as soon as possible?

Please confirm you have received this email.

Thank you.

Mary

Mary M. Lewis, RN, BSN
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Phone: 301-796-0941
Fax: 301-796-9899
Email: Mary.1.Lewis@fda.hhs.gov

3/10/2009



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-360

INFORMATION REQUEST LETTER

GlaxoSmithKline Consumer Healthcare, L.P.
Attention: Iris H. Shelton
Assistant Director, Regulatory Affairs
1500 Littleton Road
Parsippany, NJ 07054-3884

Dear Ms. Shelton:

Please refer to your July 18, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Commit® (nicotine polacrilex) Mini Mint Lozenges 2mg and 4mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Your validation report VR-C-1927-009 stated that Method C-1927.08 is the method for the determination of nicotine degradation products and impurities for the proposed drug product. However, Method C-1927.08 could not be located. Please clarify.
2. Your proposed dissolution acceptance criteria for Commit Mini lozenge are unacceptable. Please follow the principle used in the original Commit Lozenge (NDA 21,330) to establish the dissolution acceptance criteria at _____ This specification should be included for the release and the stability study. b(4)
3. Provide a sample of container/closure system for the proposed drug product.
4. Please note that a separate deficiency letter has been also communicated to the holder of DMF / _____ b(4)

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Mary Lewis, Regulatory Project Manager the Office of New Drugs (Mary.1.Lewis@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Moo-Jhong Rhee
12/19/2008 04:25:27 PM
Chief, Branch III